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Chapter 7

Dosimetric impact of intra-fraction motion during high dose rate stereotactic vertebral radiotherapy using flattened and flattening filter free beams

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Abstract

Purpose: We studied the possible dosimetric impact of relatively short duration intra-fraction shifts during RapidArc (RA) delivery for vertebral stereotactic body radiotherapy (SBRT) using flattened (FF) and flattening filter free (FFF) beams.

Methods and Material: RA plans, each with 2-3 arcs, were generated for 9 patients using 6 MV FF and 10 MV FFF beams with maximum dose rates of 1000 and 2400 MU/min respectively. A total of 1380 plans were created to estimate the dosimetric consequences in target and spinal cord volumes caused by intra-fraction shifts during one of the arcs. Shifts of 1-5 mm for periods of 5-30 seconds (s) were modelled during a part of the arc associated with high doses and steep dose gradients.

Results: For FFF plans, shifts of 2 mm over 10s and 2 mm over 30s, could increase spinal cord D_{\max} by up to 6.5% and 13% respectively. Dosimetric deviations in FFF plans were approximately 2-fold greater than in FF plans. Reduction in target coverage was <1% for 83% and 96% of the FFF and FF plans respectively.

Conclusion: Even short duration intra-fraction shifts can cause significant dosimetric deviations during vertebral SBRT delivery, especially when using very high dose rate FFF beams and when the shift occurs in that part of the arc delivering high doses and steep gradients. The impact is greatest on the spinal cord and its planning-at-risk volume. Accurate and stable patient positioning is therefore required for vertebral SBRT. At least 2 arcs should be considered to allow additional opportunities for positional verification and correction between arcs.

Introduction

Vertebral metastasis are relatively common in patients with metastatic cancer [1], and conventional radiotherapy delivered using a single fraction of 8 Gy, or 20-30 Gy delivered in 5-10 fractions are frequently used. Although these are useful treatment schemes for palliation, there remains room for improvement [2] and stereotactic body radiotherapy (SBRT) is increasingly being explored for this indication [3]. SBRT involves delivering high radiation doses to the tumor while limiting spinal cord doses by creating steep dose gradients between target and organs at risk (OAR). Consequently, accurate patient positioning before and during treatment delivery is important, as even shifts of less than 2 mm can be clinically important [4,5]. Reported delivery times for complex, high-dose vertebral SBRT vary widely, between about 10 and 90 minutes, depending on the treatment machine and technique [6-8]. Frequent position checks and corrections approximately every 5 minutes or less, have been recommended to correct non-random intra-fractional target and critical structure motion [9].

Since the introduction of volumetric modulated arc therapy including RapidArc (Varian Medical Systems, Palo Alto, CA) in 2008, rotational delivery on a linear accelerator has been widely adopted by many institutes. This technique permits fast delivery of highly conformal dose distributions [7]. Recently, RapidArc delivery using flattening filter free (FFF) beams that permit very high dose rates has been clinically introduced [10]. At 2.400 MU/min, in 3 seconds, a small field can deliver a dose up to 1 Gy and RapidArc using FFF beams can now deliver fraction doses of up to 16 Gy for vertebral SBRT within 4 minutes [11].

There have been previous reports on the dosimetric impact of shifts during vertebral SBRT delivery [4,5,12], however, they were based on the assumption that a given shift or setup error lasted for the entire fraction. The latter situation is unlikely to reflect the clinical scenario [13]. With the use of different on-board imaging modalities [6,7,12,14], patient setup can be verified and adjusted before irradiation, in between delivery of multiple beams or arcs and after treatment. Some systems also permit imaging during beam-on (e.g. CyberKnife [6]). Therefore, small shifts that last less than the complete treatment of one fraction (and which may go undetected on most treatment platforms) or detectable shifts, such as sudden larger, transient movement, perhaps as a result of pain or coughing which may occasionally occur, can lead to unquantifiable differences between planned and delivered dose. The purpose of this study was to investigate the potential dosimetric impact of all such shifts during vertebral SBRT. Effects of different dose rates and variation in the extent and duration of shifts were assessed. To the best of our knowledge, no previous reports have evaluated the impact of intra-fraction patient motion in this way, using fast, volumetric

modulated arc therapy as the delivery mode, and they have also not compared the relative impact of a given shift when using high (flattening filter, FF), or very high dose rate (flattening filter free, FFF) beams.

Methods and Materials

Treatment plans of nine SBRT patients, clinically treated with RapidArc using flattened beams and a maximum dose rate of 1000 MU/min on the Novalis TxTM, were selected for this planning study. The fractionation schemes used were 1 fraction of 16 Gy ($n = 3$), 2 fractions of 10 Gy ($n = 3$), and 3 fractions of 9 Gy ($n = 3$), all allowing up to 150% of the prescribed dose in the PTV. Details of target delineation and planning objectives have been reported previously [7]. In short, the gross tumor volume (GTV) or anatomical target region were delineated and the planning target volume (PTV) was generated by adding a 2 or 3 mm margin (not extending into the spinal canal). The spinal cord, cauda equina or thecal sac (collectively referred to as ‘spinal cord’) were delineated and a planning organ at risk volume, (PRV), was created by adding a 2 mm margin within which the dose gradient was limited. The planning objective was to deliver the prescription dose to 90% of the PTV, while adequately sparing the nearby critical structures, particularly the spinal cord and delivering a heterogeneous dose to the target volume.

A new RapidArc SBRT plan optimized using FFF beams was created for each patient. Identical planning constraints and collimator settings were used for the FFF and the original FF plans. Previous work showed no significant dosimetric differences between the 2 techniques [11]. Figure 1 illustrates the typical dose distributions and dose profiles of a FF and FFF plan. Each plan consisted of two or three separate arcs, optimized simultaneously using the Eclipse treatment planning system (version 10, Varian Medical Systems, Palo Alto, CA). Dose calculations were carried out using the Anisotropic Analytical Algorithm (AAA10.0.28) with a grid resolution of 2.5 mm, taking into account heterogeneity correction. Our institutional policy is to avoid using arcs with prolonged delivery times of > 3 minutes in order to allow for frequent patient position verification with imaging between the arcs. Consequently, FF plans for most patients were generated using 3 arcs. For FFF plans, the 3rd arc was not necessary as delivery took < 2 minutes per arc.

A total of 1380 plans were created. In order to evaluate the dosimetric impact of various types of intra-fraction movement, shifts of 1, 2, 3 and 5 mm over periods of 5, 10 and 30 seconds each were simulated. For each patient, one arc from the treatment plan was selected and divided into 20 small segments ($\sim 18^\circ$ per segment), each of which was calculated

separately (Fig. 2). At a gantry rotation that delivered high doses and exhibited steep dose gradients close to the spinal cord (defined as a large dose difference between the spinal cord and a 5 mm ring structure constructed around it), a sub-segment of 5 seconds was created. This sub-segment was shifted 1, 2, 3 or 5 mm along each axis ($\pm x$, $\pm y$, $\pm z$) relative to the isocenter and re-calculated. The shifted sub-segment was subsequently combined with the rest of the arc assuming that there was no further deviation from the planned position. The dose from the resulting arc was combined with that from the remaining arc(s), to generate the dose for the entire fraction. The dosimetric impact for one fraction was derived by comparing the plan with the arc containing a misplaced sub-segment to the original plan. The process was repeated with shift durations of 10 and 30 seconds. As different doses were delivered to the spinal cord during different segments of an arc (Fig. 2), for 2 patients, the dose deviations to the spinal cord due to intra-fractional shift of 3 mm over 10 seconds were also evaluated for different segments of the entire arc.

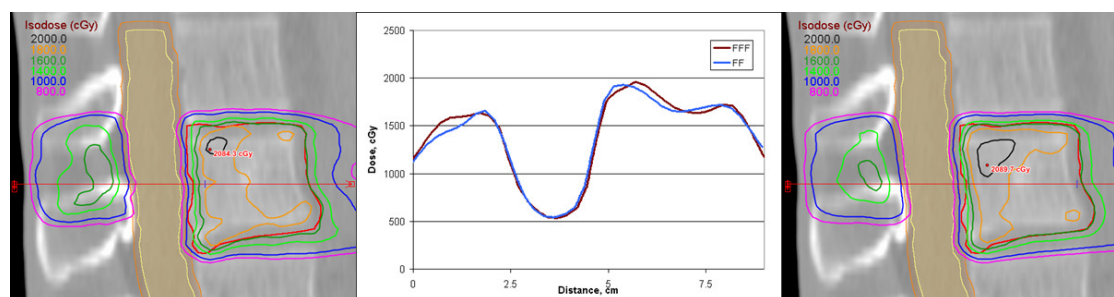


Figure 1. Dose distributions of a FFF (left) and FF (right) vertebral SBRT plan of patient 2. The planning target volume is outlined in red. The graph (middle) shows dose profiles of both plans in one sagittal plane.

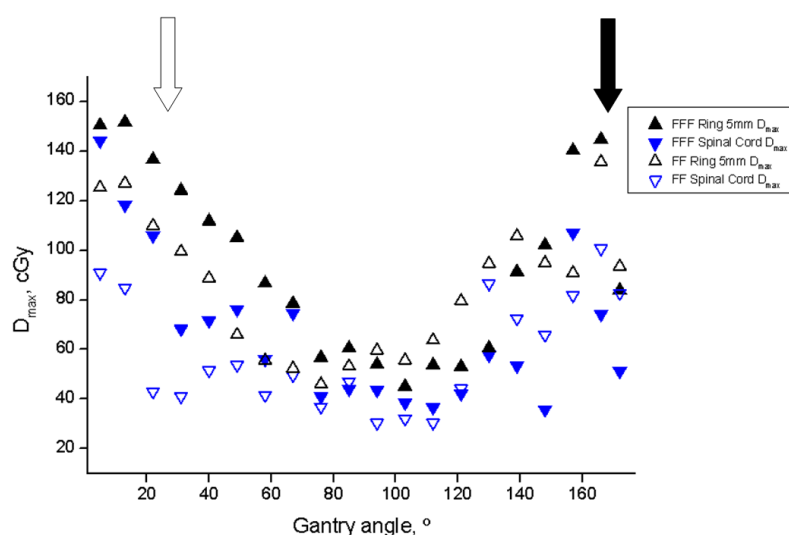


Figure 2. Doses per segment delivered to the spinal cord and the 5 mm ring structure of patient 1 during one entire arc divided into 20 discrete segments. The filled and empty arrows indicate the segments selected for FFF and FF analysis, respectively.

Dosimetric data including V_{GTV} and V_{PTV} (volume fraction of GTV and PTV encompassed by the prescription dose), and maximum dose (D_{max}) to the spinal cord and its PRV, were derived from dose volume histograms. The averages D_{max} for spinal cord and PRV for all 9 patients were 12.5 ± 3.8 Gy and 16.2 ± 3.6 Gy. For V_{GTV} and V_{PTV} , deviations in volume encompassed by the prescription dose due to the shift were noted whilst for spinal cord and its PRV the changes in D_{max} were noted.

Results

Figure 3 illustrates the deviations in spinal cord D_{max} caused by intra-fraction shifts of 1, 2, 3, and 5 mm over 5, 10 and 30 seconds in all 6 directions for all 9 cases planned using both FF and FFF beams. The dosimetric deviations were more pronounced in the lateral and anterior-posterior directions. For shifts in some directions, the maximum dose to the spinal cord became lower than in the original plans. More than 60% of the shifts results in a higher D_{max} . For a shift of 2 or 3 mm lasting 10 seconds, the maximum increase in spinal cord D_{max} for a single fraction of all 9 FFF plans ranged from 0.6 - 6.5% and 1.3 - 11%, or 3 - 32 and 6.3 - 60 cGy, respectively. If these shifts lasted 30 seconds, the maximum increments for 2 mm and 3 mm were 2.3 - 13% and 3.9 - 21.4%, respectively. The averages of the maximum deviations in spinal cord D_{max} under each simulated scenario, e.g. 1 mm shift over 5s, for all 9 cases planned using FFF and FF beams are shown in Fig. 4. FFF plans consistently exhibited larger dose deviations when compared to FF plans, especially as the magnitude or the time of the shifts increased ($p < 0.0001$, Wilcoxon signed rank test). The magnitude of the deviations in D_{max} of the spinal cord and its PRV was similar.

The changes observed in percentage of dose coverage to V_{GTV} and V_{PTV} were smaller. For shifts of up to 3 mm over 10 seconds, the maximum decrements in V_{GTV} and V_{PTV} observed for all 9 patients were on average $< 0.8\%$ and $< 0.4\%$ for FFF and FF plans, respectively. If the shifts extended up to 30 seconds, the deviations were still $< 1.6\%$ and $< 0.8\%$ for FFF and FF plans, respectively. Of the 648 FFF plans stimulated for all scenarios, only 12% and 17% of the plans exhibited decrement of $> 1\%$ in V_{GTV} and V_{PTV} , respectively, compared with 3.2% and 4% for the corresponding 648 FF plans.

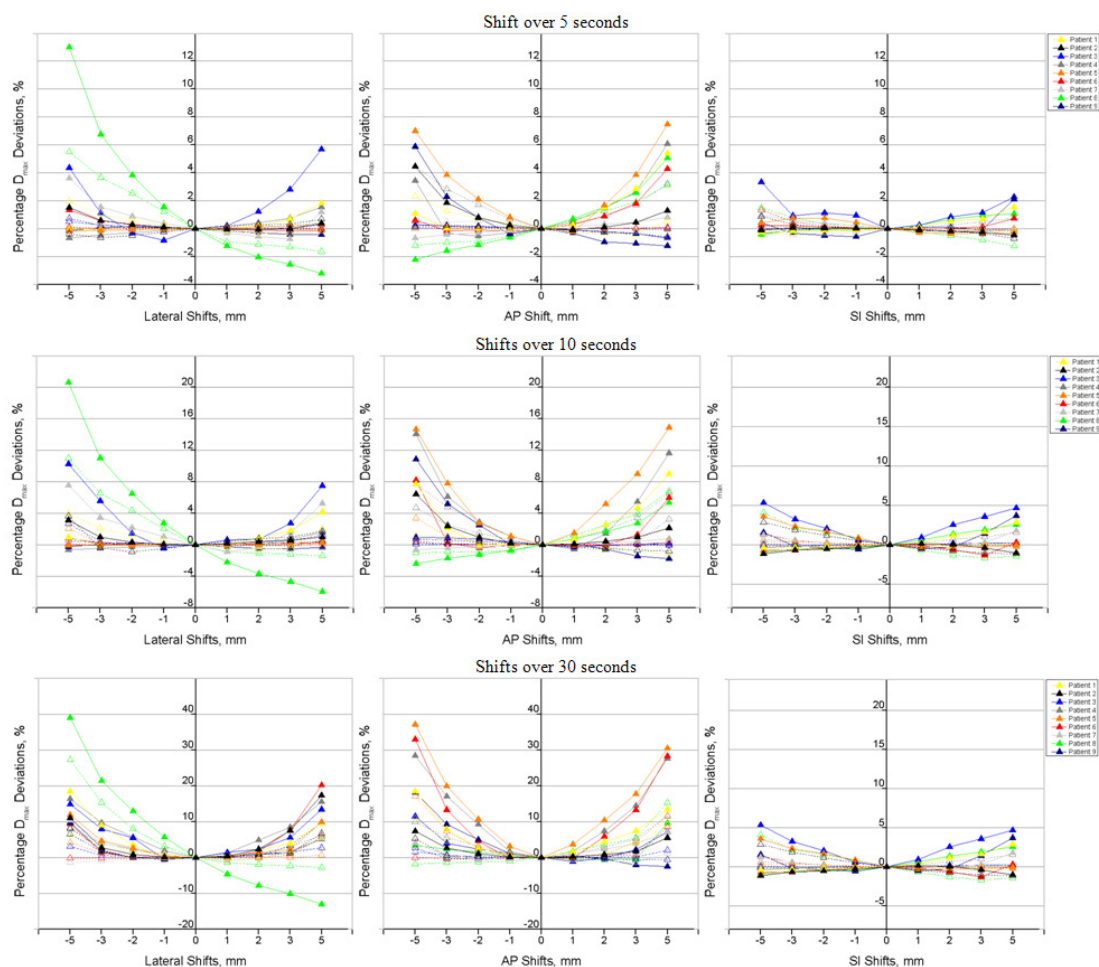


Figure 3. Dosimetric deviations in D_{max} of spinal cord caused by intra-fraction motion of 1, 2, 3 and 5 mm in lateral (RL), anterior-posterior (AP), and superior-inferior (SI) direction over 5, 10 and 30 seconds. Deviations were calculated by comparing the FFF (solid line, filled triangle) and FF plans (dashed line, empty triangle) containing an arc with a misplaced segment to the original plan of one fraction.

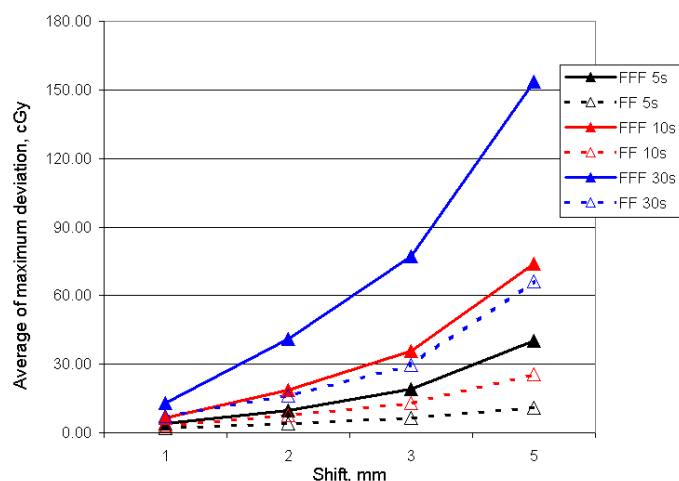


Figure 4. Average of maximum deviation in spinal cord D_{max} for all 9 patients caused by intra-fraction shifts of different durations and magnitudes.

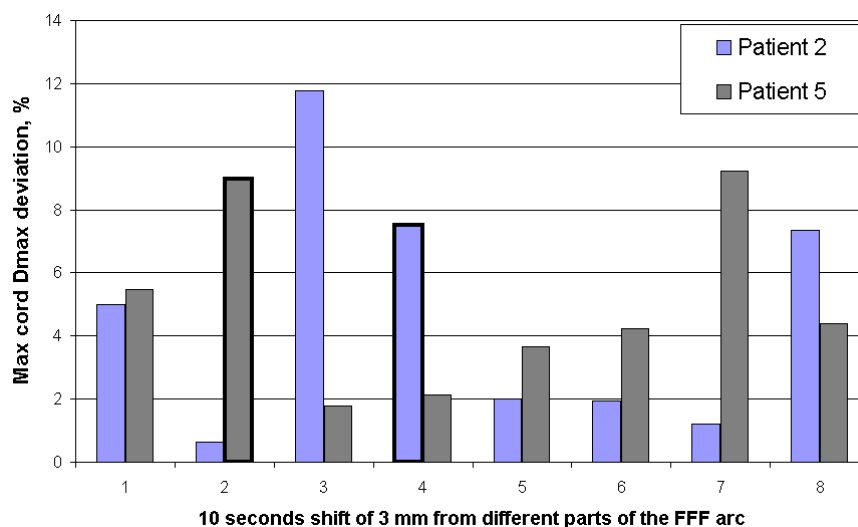


Figure 5. Maximum increments in spinal cord D_{\max} for patient 2 and 5 caused by 3 mm shifts for 10 seconds, varies between different segments of one FFF arc. The selected bars indicate the segment chosen for the analysis presented in Figure 3.

An additional 84 plans were created to examine the dose deviation to the spinal cord due to a shift of 3 mm for 10 seconds occurring during different sections of a single FFF arc (Fig. 5). For a shift occurring at any given section of the arc, the maximum dose deviations observed over all 6 directions are presented. The selected bars (thick black outline) indicate the maximum dosimetric deviation (after a single 3 mm shift for 10 seconds) for the sub-segments chosen for the analysis presented in Fig. 3. Fig. 5 shows that if this shift had occurred at other sections of the arc, the magnitude of deviation in spinal cord D_{\max} could be even larger.

Discussion

While fast delivery using RapidArc [7] reduces the time available for patient movement, motion can still occur. The present study aimed to demonstrate the possible dosimetric impact of different magnitudes of patient motion lasting various lengths of time, during rapid vertebral SBRT delivered with volumetric modulated arc therapy using flattened or FFF beams. In combination with very high dose rate FFF beams, transient intra-fraction motion, lasting less than the duration of a single arc, can in some cases lead to significant deviations from the treatment plan. We evaluated intra-fraction shifts lasting for various periods of time in order to simulate different types of patient movement during an arc and the time taken to identify the motion and interrupt the beam.

For vertebral SBRT delivery, Wang et al recommended that translational and rotational tolerances should be ≤ 1 mm and 2° respectively [4] and Guckenberger et al reported that a 2 mm translational error, for the entire treatment, could result in a 35% increase in dose

received by part of the spinal cord [5]. Our results showed that after a shift of 3 mm for 10 seconds it was possible for the spinal cord D_{\max} to increase by up to 11%. Our clinical experience, based on imaging before and after each arc, is that the vast majority of translational spine shifts (x, y or z) are ≤ 1 mm, even without external immobilization, and that shifts of 2 mm, although uncommon, are occasionally observed. If such shifts go undetected during beam-on, our data suggests that a 2 mm shift for 30 seconds could increase the D_{\max} to the spinal cord by up to 8% and 13% for an FF and FFF plan respectively. And for a larger sudden shift, as could perhaps occur during a coughing episode or experienced sudden pain, we showed that the spinal cord D_{\max} could increase by up to 4 – 13% using FFF delivery for a shift of 5 mm for only 5 seconds. The dosimetric impact of a given shift was approximately two times larger for FFF than for FF delivery. However, note that if such a shift was present during the entire fraction, the dosimetric impact would be similar for FFF and FF, provided the plans were clinically comparable [11].

Although segments that exhibited a high dose gradient between the spinal cord and 5 mm ring structure were selected for analysis, the dosimetric deviation (Fig. 3) did not necessarily represent the worst-case scenario (Fig. 5). Apart from the distance and duration of shifts, the magnitude of dosimetric deviations is also dependent on the direction of the shift, the angle of the incoming beam during arc delivery, and the distance between target and OAR. Unlike IMRT, volumetric modulated arc therapy delivers dose as the gantry rotates. Therefore, for any given shift during beam-on, the dosimetric impact is spread out because dose is delivered over consecutive gantry angles. The risk of significant dosimetric variation may therefore be higher for static IMRT delivery.

Reductions in target coverage were smaller because the physical volumes were larger than those of the spinal cord. For most investigated plans, the deviations to both of the V_{GTV} and V_{PTV} were $< 1\%$. With a PTV margin of 2 - 3 mm, shifts of 1 - 2 mm should not substantially influence GTV coverage, but where the spinal cord is in contact with the GTV for example, no PTV margin is applied and some shifts may immediately lead to underdosage of the target.

Although most conventional treatment platforms are fitted with integrated imaging modalities, frequent spine imaging for positional verification during beam-on is not possible except on the CyberKnife system [6], however, SBRT treatment can take a relatively long time to deliver in comparison to RapidArc and imaging is typically intermittent. Consequently, small shifts of 1 - 2 mm may go unnoticed on many contemporary treatment platforms and can only be corrected if they are detected by imaging between different fields or arcs. For this reason, we recommend volumetric modulated arc therapy delivery of

vertebral SBRT using ≥ 2 arcs for each fraction and performing online imaging and positional correction between arcs. This distributes the dose between the arcs and may help to mitigate the dosimetric impact of intra-fraction motion.

We perform vertebral SBRT using a positional tolerance of 1 mm and 1° . We use the Novalis TxTM and the TrueBeamTM platforms. The former has an infrared tracking system, however we do not feel that this can confidently identify spine motion of $\leq 1 - 2$ mm, since the relationship between the external markers and the spine at any given time is not quantified. Although it suffers from the same limitations, on the TrueBeam we are currently performing positional monitoring with the RPM (Real-time Position ManagementTM) box and interrupting the beam when a pre-set displacement is exceeded. Presently, we only use routine external immobilization for cervical/upper thoracic spine SBRT [7,15]. Although immobilization devices are often used in vertebral SBRT, it is important to realize that intra-fraction motion of at least 2 - 3 mm can still occur [13,16,17], and that the importance of accurate and frequent positional verification is not reduced.

Although a potential limitation of the present study is that we only studied the dosimetric deviations caused by translational shifts, at least one report of positioning errors in vertebral SBRT has shown that dose variations were greater for translational than rotational shifts [12]. In addition, we studied the impact of a single shift during the fraction and assumed that the remainder of the dose was delivered precisely as planned, rather than the more likely scenario of a series of consecutive, slightly different positions. However the purpose of the present study was to highlight the potential impact of clinically relevant, relatively short-lived motions. Although we showed that the use of FFF beams may exacerbate the dosimetric impact of intra-fraction motion, it is also possible that shorter delivery times might help to mitigate motion [13]. Nonetheless, frequent patient monitoring and timely positional corrections are needed to avoid significant dosimetric deviations during beam-on.

Conclusion

Fast FFF delivery of IMRT plans using RapidArc enables high dose fractions to be completed in only a few minutes. Although this might reduce the chance of intra-fraction motion compared to more prolonged treatments, it enhances the dosimetric impacts of possible shifts over short period of time. Therefore, it also requires more frequent imaging to ensure accurate patient positioning. Rotational delivery using at least 2 arcs is recommended to allow positional verification and correction between arcs.

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